THE SYMPTOM-COMPLEX OF CENTRAL NEURITIS

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It is only within recent years that central changes have been demonstrated in connection with peripheral lesions in polyneuritis. These observations have greatly widened our conception of the various toxic types of polyneuritis, and in these central changes there was found an explanation for the frequently associated mental condition, which had previously proved so perplexing. These cell changes are usually of some type of chromatolysis, with a disappearance of the Nissl granules and the neurofibrils, the type of change that is seen in the ventral horn cells of the spinal cord and medulla, when the axon is cut or destroyed. It is known therefore as the axonal reaction. Associated with this axonal cell change, there is a degeneration of the myelin sheaths, usually systematic in distribution and involving mainly the pyramidal tracts in the brain and spinal cord, and the columns of Goll and Burdach. The cells involved are principally the large and small motor cells of the cortex, the nuclei of the medulla, the cells of Clarke's column and the anterior horn cells. All of these cell and fiber changes can be demonstrated in the brain and cord in cases of peripheral neuritis, thus showing that the peripheral symptoms are merely one expression of a general toxic disorder. In some cases no central changes can be found in a peripheral neuritis, in others, these central changes are abundant. The points to which we wish to call particular attention in this paper, are those conditions in which the systemic degenerations are entirely of central distribution without any peripheral neuritis, and in which the clinical symptom-complex is so typical, that frequently an ante-mortem diagnosis can be correctly made. Many of these cases came to autopsy, as the disorder is purely a terminal one, arising mainly on the basis of certain toxic, cachetic or depressive disorders.

In 1901 Adolf Meyer and later I in 1906 called attention to this combined neurological and mental condition, the former as the end stage of certain depressive psychoses, the latter, as a hitherto undescribed form of alcoholic neuritis. Because of the purely central distribution of the cell and fiber changes without any sign of peripheral neuritis, the name central neuritis was proposed by Meyer for this symptom-complex. The name was retained by me in my alcoholic cases, as it expressed so admirably the neurological aspect of the affection. Anatomically there was more or less marked axonal reaction of the large motor cells of the brain and spinal cord, the nuclei of the medulla and of Goll and Burdach, with corresponding systemic degeneration of myelin sheaths of the pyramidal tracts, fillet and the posterior columns of the cord; chemically, cholin as a myelin degeneration product could be demonstrated in the cerebrospinal fluid and the nerve tissue itself, while the urine showed hyperindicanuria and sometimes acetonuria.

Briefly the clinical condition was characterized by diarrhea, emaciation, twitchings or rigidity of the extremities, some fever and some changes in the reflexes. The symptom-complex was purely a terminal episode. At first demonstrated as the end picture of certain depressive and cachectic disorders, I later found it to occur as a pure condition in certain alcoholic psychoses in which peripheral neuritis was absent. For this group of cases I proposed the name of alcoholic central neuritis, in contradistinction to the peripheral variety. However, since this axonal cell change has been found in other distinctly toxic states, it will be well to summarize the literature on the subject and attempt to correlate the anatomical findings with the clinical picture. A remarkable unity will be found to underlie this diverse etiology. As practically all the cases of central neuritis have occurred in emaciated and debilitated individuals, it will be of interest to first discuss the changes in the nervous system found in experimental inanition. Monti found that while the thin dendrites of the pyramidal cells vanished, the axis cylinders with their collaterals remained intact. Schaffer (3) found vacuolation, degeneration of the cell nucleus and some chromatolysis, the latter usually beginning around the nucleus. Hatai (4), in examining the brains of starved white rats, could find no alteration in the Nissl bodies. It will be observed that nothing resembling the axonal reaction could be demonstrated in these inanition experiments.

Sims (5) in two cases of acute polyneuritis with a typical mental disorder, one of the cases showing twitching of various muscle groups, found an axonal reaction in the cortex, anterior horn cells, Clarke's column, and the cranial nerve nuclei. Both Soukhanoff and Marinesco also found this axonal reaction in the motor cells of the cortex in cases of peripheral neuritis associated with mental symptoms. The same cell change has also been found in the end stages of dementia præcox, associated with emaciation and rigidity. Here it must be interpreted, not as the essential anatomical basis of the disease, as some observers have done, but as a purely secondary cell change, of terminal origin. The same cell alteration with central system degeneration has also been demonstrated in amaurotic family idiocy, and it is well known how frequently emaciation is an accompaniment of this disease. Bolton found the axonal reaction in the cells of the vagus nucleus in diphtheria. He appears, however, not to have examined for fiber degeneration by the Marchi reaction. Both Bikeles (6) and Thomas (7) demonstrated acute central degenerations in post-diphtheritic paralysis. The former found posterior column degeneration, especially marked near the posterior root entrance zone. Thomas found degeneration in the posterior columns of the cord, in the pons, superior cerebellar peduncle, formatio reticularis, cortex and pyramidal decussation. None of these cases showed any rigidity or twitchings, while the nerve cells were designated as normal. This lack of cell change is difficult of explanation, unless we assume that the nature of the toxic process on the myelin sheaths was so rapid that the nerve cells could not assume any characteristic change before death supervened.

There are certain other toxemias, due to poisons generated in the system or introduced from without, that may cause this axonal reaction. Tschernischeff (8) found, in two cases of fish poisoning with severe gastrointestinal symptoms and progressive weakness, but without any disorder of consciousness, a diffuse chromatolysis in the cells of the medulla, the vagus nucleus, pons, corpora quadrigemina and cortex. Nichols (9), in cases of typhoid fever and in experimental infection with the typhoid bacillus, found a typical axonal reaction in the motor cells of the spinal cord and of the posterior root ganglia. He believes that these changes are identical with those found in nerve cells after section, destruction or slight injury of the peripheral nerves.

More important, however, because accompanied by excellent clinical descriptions, are the investigations of E. Meyer (10) on the auto-intoxication psychoses. Here, not only was the axonal reaction marked and the changes in the cells bore a striking resemblance to those found by Bonhoeffer in delirium tremens, but the Marchi reaction showed distinct degeneration in the central convolutions and in the cerebellar worm. In an analysis of the cases, one important fact is noticeable, namely, that the axonal change or the fiber degeneration was found only in those cases which resembled clinically the picture of central neuritis. These cases showed emaciation, diarrhea, fever, rigidity, spasmodic movements and jerky tremor of the arms and legs, grimacing, mumbling speech, changes in the reflexes, and either confusion or delirium.

In Cole's (11) cases of alcoholic paralysis, there were muscular jerkings and rhythmical convulsive movements of the limbs. That these phenomena were of purely cortical origin and not attributable to peripheral neuritis is shown by the presence of the axonal reaction in all the cells of the spinal cord and the cortex, with degeneration of the pyramidal tracts, posterior columns, ponto-thalamic fibers, cerebellar tracts, etc. In the case of mental confusion reported by Ballet and Faure (12), the axonal reaction was found in nearly all the Betz cells, while clinically the cases showed many features of a central neuritis, such as muscular rigidity, emaciation, increasing weakness and sudden collapse. The authors interpret the condition as a kind of parenchymatous encephalitis.

Orr (13), in studying certain phases of the acute psychoses, found a general axonal reaction with central degenerations in cases of melancholia, acute delirium and depressive delirious states. One of the cases had stuporous episodes, another showed difficulty in swallowing and had twitching of the arms and legs. In an investigation of the nerve cells in thirty-three cases of insanity, Turner (14) found in five of these cases an axonal reaction of the Betz cells, the larger pyramids and the anterior horn cells, with degeneration of the posterior columns and the pyramidal and direct cerebellar tracts.

This axonal cell change has also been found in the cerebral cortex secondary to lesions of the internal capsule (Marinesco), in tetanus (Schupfer), in phosphorus poisoning (Rossi), acute delirium (Carrier), in Landry's paralysis (Worcester), in delirium tremors (Bonhoeffer and Ewing), in pellagra intoxication (Righetti), and also in certain trypanosome infections, such as the sleeping sickness.

All of my cases were observed at the Worcester Insane Hospital. Only short summaries are given, but these present sufficient clinical, pathological and chemical detail to give a clear picture of the symptom-complex. The first four cases have already been published in full in my paper on mental disturbances of alcoholic neuritis.

CASE I.—Delirium tremens in a man of 55, of very acute onset. There rapidly supervened a slight peripheral neuritis, later deep confusion with twitchings, rigidity, tremor of the arms, double Babinski reflex, albuminuria, hematoporphyrinuria. The patient died a week after the onset of the above symptoms and although an autopsy could not be obtained, yet the clinical course seemed to justify the diagnosis of central neuritis.

CASE II.—Alcoholic depressive hallucinosis in a man of 42, with rapid emaciation, diarrhea, tremor, rigidity, twitchings. Death took place in two weeks from lobar pneumonia. Here again, although no autopsy was performed the clinical condition was that of central neuritis.

CASE III.—Alcoholic depressive hallucinosis in a man of 50, with marked episodes of fear, later emaciation and diarrhea, with rigidity, twitchings and disorders of the reflexes (exaggerated knee jerks, double Babinski). Hyperindicanuria was present. Death from broncho-pneumonia. There was an axonal reaction of nearly all the cells in the cortex and medulla, in the anterior horn cells, the cells of Clarke's column and the posterior root ganglia. Cholin was demonstrated in the cerebrospinal fluid.

CASE IV.—Alcoholic depressive hallucinosis, with episodic expansive ideas, emaciation, diarrhea, marked rigidity and explosive twitchings. Death from pulmonary tuberculosis. The above symptoms were observed for only four days before death. There was a general cortical atrophy, an axonal reaction of the cells in the frontal and paracentral regions, in the anterior horn cells and spinal ganglia. Cholin found in cerebrospinal fluid. None of the above alcoholic cases showed any of the tissue changes characteristic of general paralysis.

CASE V.—Melancholia in woman of 44, with anemia, agitation, depression, resistance, somatic delusions, later emaciation and diarrhea, increased muscular tension in the limbs, slight fever, severe rigidity of right fore-arm, tremor of chin and lips, dry seborrhea of feet, hands and face, exaggerated reflexes, right ankle clonus, no Babinski, unequal pupils, frequent jerkings of fingers of right hand. Albuminuria and hyperindicanuria. Death from broncho-pneumonia. The anatomical examination showed the axonal reaction in the small pyramids and Betz cells of both right and left paracentrals, in the first right and left frontal convolutions, medulla, anterior horn cells of the spinal cord and posterior root ganglia. There was a Marchi reaction of the motor fibers. The cells showed little pigmentation and only a moderate amount of swelling. Cholin was present in the cerebro-spinal fluid.

Case VI.—Dementia præcox in a woman of 41. There were residuals of an old anterior poliomyelitis. The terminal episode was indolence, unproductiveness, a filthy dilapidated manner, diarrhea, emaciation, severe rigidity and general twitchings, exaggerated reflexes, fever, no leucocytosis. In the urine there was demonstrated acetone, diacetic acid, albumin and a large amount of indican. Death from broncho-pneumonia. The brain showed nothing gross. The right anterior horn of the cord was smaller than the left. Cholin was found in the blood and cerebro-spinal fluid. There were no toxic products found in the urine by the method of Stass-Otto (injection of the different portions into white rats) and no alkaloidal reactions in the different portions. In the first left frontal convolution, scarcely a cell with the granules in their normal stitochrome arrangement could be demonstrated. Nearly all the large and small pyramidal cells were in a state of axonal reaction. In the paracentrals all the pyramidal, particularly the large Betz cells, showed a severe axonal reaction. Some of these latter were pigmented.

Case VII.—Senile depressive paranoic state in a man of 62. The terminal state was gangrene of the foot, toxic nephritis with waxy casts and hyperindicanuria, increasing weakness and emaciation, diarrhea, stuporous episodes, tremor of the arms, twitching of the fingers and lower arm muscles and rigidity of the arms and neck. Later the legs began to twitch and the expression became haggard and drawn. There was ptosis of the right eyelid, sluggish pupils, exaggerated knee jerks, no Babinski reflex. Death took place from lobar pneumonia. The autopsy disclosed a general arterio-sclerotic brain atrophy. Nearly all the pyramidal and Betz cells of the paracentral and frontal lobes, likewise the cells of the posterior spinal ganglia, showed an axonal reaction with only a moderate amount of swelling and pigmentation. In only a few cells was the arrangement of the granules normal. There was no cholin in the cerebro-spinal fluid or brain substance.

Case VIII.—Dementia præcox in a woman of 40, with a persecutory hallucinosis, mutism, fear and marked perplexity. For a month previous to death there was almost continual diarrhea; later there developed explosive muscular twitchings of the face, neck and all the limbs. These twitchings were almost continual in character and were increased in intensity by any external stimulus. There was rigidity and spasticity of the right leg, staring expression, fever, albuminuria and hyperindicanuria, exaggerated knee and Achilles jerks, ankle clonus and double Babinski. Death from lobar pneumonia. There was some atrophy of the frontal and temporal convolutions, while cholin was found in the brain and cerebro-spinal fluid. The pyramidal cells were in a state of axonal reaction, more marked on the right.

CASE IX.—Melancholia in a woman of 45, with stupor and resistiveness. For several days before death there were noted twitchings and marked rigidity. Death from pulmonary tuberculosis. Axonal reaction of the pyramidal and Betz cells of the frontal and paracentral regions, also in anterior horn cells. No cholin was found in the cerebro-spinal fluid.

CASE X.—Melancholia with marked depression, seclusiveness and suicidal attempts. Death from exhaustion. No rigidity or twitchings. Axonal reaction of the cortical cells.

CASE XI.—Carcinoma of the uterus with cachexia and emaciation. Axonal reaction of the cortical cells.

CASE XII.—Carcinoma of the uterus and rectum with emaciation and cachexia. No rigidity or twitchings. Axonal reaction.

CASE XIII.—Delirium with rigidity and twitchings. Axonal reaction.

CASE XIV.—Senile dementia with depression, emaciation, diarrhea and stuporous episodes. No rigidity or twitchings. Axonal reaction of the cortical cells.

CASE XV.—Alcoholic Korssakow's disease in a man of 43. Death after a rapid course, with rigidity, twitchings, severe diarrhea and rapid emaciation. Axonal reaction of the pyramidal and Betz cells.

CASE XVI.—Katatonia in a woman of 46. Protracted excitement, fainting attacks, marked loss in weight with progressive emaciation, diarrhea and increasing weakness. Normal pupils and reflexes, no tremor, twitchings or rigidity. The gross appearance of the brain was normal. About a third of the large pyramidal cells were in axonal reaction; some were greatly swollen.

CASE XVII.—Manic excitement with delirious episodes in a woman of 44. Later there developed emaciation, severe diarrhea, fever with moderate leucocytosis, continual mumbling and grimacing, difficulty in swallowing and a haggard expression. In addition there was extreme resistance and rigidity of the neck, arms and legs, tremor and twitching of the hands and exaggerated reflexes. The urine contained an abundance of indican and showed a positive diazo reaction, but there was no other evidence of typhoid fever. Death from chronic enteritis. No autopsy.

CASE XVIII.—Delirium in a middle aged woman, with auditory and visual hallucinations, frontal headache, staggering gait, vertigo, fever, rigidity of arms, spasmodic jerkings and finally Cheyne-Stokes respiration. Axonal reaction.

CASE XIX.—Delirium in a man of 44, with asymboly, marked confusion, rapid physical decay and progressive weakness, rigidity of limbs and slight twitchings of left hand, ptosis of left eyelid, death from lobar pneumonia and exhaustion. No autopsy.

CASE XX.—Dementia præcox in a woman of 33, with diarrhea, progressive weakness and during the last week before death jerky twitchings of the limbs. Death from pulmonary and intestinal tuberculosis. Axonal reaction of the Betz cells.

CASE XXI.—Dementia præcox in a woman of 25, with progressive loss in weight and severe diarrhea. Death from tubercular enteritis. Axonal reaction of the Betz cells.

CASE XXII.—Dementia præcox in a woman of 22, with stuporous and restless episodes, loss in weight, diarrhea, slight fever. Death from broncho-pneumonia. Axonal reaction of the pyramidal cells.

CASE XXIII.—Alcoholic depressive hallucinosis in a woman of 41, with restless and stuporous episodes, development of absurd somatic delusions. Later loss in weight, mutism and staring expression. About a month before death there developed marked rigidity of the right arm, the limb being held in a hemiplegic position, then general, paroxysmal twitchings of the body, exaggerated reflexes, fever and death from pulmonary tuberculosis. The Nissl specimens of the cord and brain (the frontal and paracentral region) showed a marked axonal reaction of all the cells with severe swelling. Many of the nuclei were filled with small vacuoles. With the Marchi stain there were a moderate number of blackened fibers in the corona radiata. Cholin was absent from the cerebro-spinal fluid.

An analysis of the material shows the following features. Out of twenty-three cases the symptom-complex was present six times in the alcoholic psychoses (one case of delirium tremens, one of Korssakow's disease, and four of the depressive hallucinatory type), three times in melancholia, five times in dementia præcox, twice in senile depression, twice in carcinoma of the uterus, three times in acute delirium and once in manic-depressive insanity. The prominent symptoms were loss in weight, emaciation, diarrhea, muscular rigidity and twitchings. The muscular rigidity was either confined to one group of muscles or comprised an entire limb, while the twitchings varied from a slight involvement of the fingers to the entire body, sometimes explosive in character, sometimes resembling a tetanic condition. A general restlessness and tremor of the arms was also a very frequent symptom. Fever was almost always present. Stuporous episodes and staggering occasionally occurred, also mumbling, grimacing and difficulty in swallowing. In four cases (V, VII, XIX, XXIII) there were focal symptoms, ptosis of the right eyelid and rigidity of the right arm. Death took place in most cases either from cachexia, pulmonary tuberculosis or lobar or broncho-pneumonia. As a rule the reflexes were exaggerated. In several cases the pupils were unequal. Ankle clonus was observed twice, while the Babinski reflex was obtained three times. In nine cases in which an examination for cholin was made, the alkaloid was detected six times, a most convincing proof of the presence of myelin degeneration. In several cases there was a large increase of indican. Acetone and diacetic acid were detected once. In all the cases the axonal reaction was present in the brain and cord (frontal and paracentral regions, medulla, anterior horn cells, the cells of Clarke's column). None of the cases showed any of the tissue changes of dementia paralytica. In one case of depressive dementia paralytica resembling central neuritis (diarrhea, rigidity, twitchings and a lymphocytosis of the cerebro-spinal fluid) there was present a hemorrhagic pachymeningitis and histologically the cortex showed the typical tissue changes of the disease, but without any axonal reaction.

Since the symptom-complex of central neuritis is purely terminal in nature, occurring as the end-picture of certain cachetic, depressive or delirious states, recovery cannot take place. On the other hand, depressive psychoses with marked emaciation and diarrhea are frequently observed, in which neither clinically nor anatomically, can any central neuritis be demonstrated. What then are the conditions necessary for the production of central neuritis? A toxic etiology can easily be dismissed, as the presence of cholin and the findings in the urine are merely secondary. Furthermore, in one of our cases, a careful examination of the urine both chemically and physiologically, failed to demonstrate any poisonous products. The change in the nerve cells cannot be produced by inanition, for we have seen that under these conditions there is nothing resembling the axonal reaction. The symptom-complex can be fairly satisfactorily explained, however, by an application of Edinger's Ersatz-Theorie. For the maintenance of a perfect function of the nerve cell, it is necessary that the reparative power of the cell should be accurately balanced and adjusted. If the cell becomes unable to repair the loss sustained by its functional activity, a progressive degeneration of the entire neurone follows. Mott has also pointed out how in neurones in a low state of nutritional equilibrium degeneration first begins in the fine collaterals and terminals and proceeds back to the cell of origin. Now in certain psychoses, the loss in weight, diarrhea and emaciation reduces the neurone to such a low state of nutrition that it absolutely destroys its reparative power. As a result the entire neurone degenerates and the peculiar symptom-complex of central neuritis follows.

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